REMARKS

Claims 1-7 and 9-16 are presently pending and under consideration. Claim 8 has been canceled and claims 11-14 stand withdrawn from consideration as directed to a non-elected invention. Claim 1 has been amended to recite that the polycarboxylic chelating agent reduces variation in detected amounts of trypsin inhibitor caused by the presence of calcium ions in the urine. The amendment to claim 1 is supported throughout the specification, for example, at page 4, lines 21-26, and adds no new matter. Accordingly, entry of the amendment to claim 1 is respectfully requested.

Regarding 35 U.S.C. § 112, Second Paragraph

The rejection of claims 1-7, 9, 10, 15 and 16 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to point out and distinctly claim the subject matter regarded as the invention respectfully is traversed.

The Office Action asserts that it is unclear if recitation of the phrase "correlating the concentration of trypsin inhibitor with the detectable response from the cleaving of the substrate" means that the trypsin inhibitor concentration has already been determined and is simply correlated to a detectable signal or, in the alternative, if this phrase means that the signal detection is used to determine the trypsin inhibitor concentration (current Office Action; page 2). For the reasons that follow, Applicants respectfully disagree with the assertion that claim 1 is indefinite.

The Federal Circuit has made clear that definiteness of claim language must be analyzed, not in a vacuum, but in light of (1) the content of the particular application disclosure, (2) the teachings of the prior art, and (3) the claim interpretation that would be given by one possessing

the ordinary level of skill in the pertinent art at the time the invention was made. See, e.g., *In re Marosi*, 710 F.2d 799, 218 U.S.P.Q. 289 (Fed. Cir. 1983); *Rosemount, Inc. v. Beckman Instruments, Inc.*, 727 F.2d 1540, 221 U.S.P.Q. 1 (Fed. Cir. 1984); *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983); and *Atmel Corp. v. Information Storage Devices, Inc.*, 198 F.3d 1374, 53 U.S.P.Q.2d 1225 (Fed. Cir. 1999) (district court failed to consider the knowledge of one skilled in the art when interpreting the patent disclosure).

> The primary purpose of the definiteness requirement is to ensure that the claims are written in such a way that they give notice to the public of the extent of the legal protection afforded by the patent, so that interested members of the public, e.g., competitors of the patent owner, can determine whether or not they infringe. That determination requires a construction of the claims according to the familiar canons of claim construction.

All Dental Prodx, LLC v. Advantage Dental Prods., 309 F.3d 774, 779-80, 64 USPQ2d 1945, 1949 (Fed. Cir. 2002) (citations omitted).

The determination of whether a claim is invalid as indefinite "depends on whether those skilled in the art would understand the scope of the claim when the claim is read in light of the specification." *See N. Am. Vaccine, Inc. v. Am. Cyanamid Co.*, 7 F.3d 1571, 1579 (1993) (citation omitted).

Applicants respectfully submit that the skilled person, reading claim 1 in light of the specification, would understand that the claimed "assay for trypsin inhibitors in urine" is directed to the detection of trypsin inhibitor in the urine sample as is explained throughout the specification (see, for example, page 5, lines 14-16). As proof of principle, the specification teaches correlating the concentration of trypsin inhibitor with the detectable response from the cleaving of the substrate, for example, in Example III, and shows that the reflectance decode value is directly proportional to the trypsin inhibitor concentration. Thus, the specification exemplifies the utility of the assay for

detecting trypsin inhibitor in urine. It is respectfully submitted that the alternative suggested in the current Office Action, an assay for trypsin inhibitor in urine where the trypsin inhibitor concentration has already been determined and is simply correlated to a detectable signal, is not a reasonable interpretation of claim 1 by one skilled in the art in light of the specification. Since the disclosed purpose of the assay for trypsin inhibitor is the detection of trypsin inhibitor in the urine, the purpose for the assay would be defeated if the trypsin inhibitor concentration was already known prior to the assay.

It is respectfully submitted that a skilled person familiar with the specification would not assume that the purpose of the assay is to correlate an already known trypsin inhibitor concentration to a detectable signal. The detectable signal has no purpose but for determining the trypsin inhibitor concentration.

In summary, the Federal Circuit decisions, discussed above, demonstrate that when examining whether claim language satisfies the requirements of § 112, second paragraph, one must examine the claims as a whole in light of the specification and the prior art and do so as one of ordinary skill in the art at the time the invention was made. Applicants submit that the ordinarily skilled artisan, at the time the application was filed, in view of the teachings in the specification and contemporary art-knowledge, would have viewed claims 1-7, 9, 10, 15 and 16 as sufficiently clear and definite and that they do particularly point out and distinctly claim the subject matter of the invention. Accordingly, Applicants respectfully request reconsideration and removal of the rejection of claims 1-7, 9, 10, 15 and 16 under 35 U.S.C. § 112, second paragraph.

Rejection under 35 U.S.C. § 103(a)

The rejection of claims 1-4, 7, 9, 15 and 16 under 35 U.S.C. § 103(a) as being unpatentably obvious over United States Patent No. 5,856,117 to Uenoyama et al. in view of Ausubel, *Current Protocols in Molecular Biology*, and further in view of United States Patent No. 5,384,247 to Berry et al. is respectfully traversed.

Applicants argued in their previous Response filed December 22, 2003 that Uenoyama et al. discloses a method for assaying amount of trypsin inhibitor in a urine sample which requires the addition of calcium to the assay medium, while Applicants' claimed method discloses that the polycarboxylic chelating agent is added to reduce variation in detected amounts of trypsin inhibitor caused by the presence of calcium ions in the urine. In responding to Applicants' arguments, the current Office Action points out that the feature on which Applicants' arguments rely is not recited in the base claim. As amended herein, base claim 1 recites that the polycarboxylic chelating agent reduces variation in detected amounts of trypsin inhibitor caused by the presence of calcium ions in the urine. Therefore, Applicants submit that the rejection has been rendered moot.

To establish a *prima facie* case of obviousness, the Office must satisfy three requirements. First, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, must contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference or to combine references. See *Karsten Mfg. Corp. v. Cleveland Gulf Co.*, 242 F.3d 1376, 1385, 58 U.S.P.Q.2d 1286, 1293 (Fed. Cir. 2001); *C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1352, 48 U.S.P.Q.2d 1225, 1232 (Fed. Cir. 1998); *Northern Telecom v. Datapoint Corp.*, 908 F.2d 931, 934, 15 U.S.P.Q.2d 1321, 1323 (Fed. Cir. 1990). Second, the proposed modification of the prior art must have had a reasonable

expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. In other words, a hindsight analysis is not allowed. See *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991); *In re Erlich*, 3 U.S.P.Q.2d 1011, 1016 (Bd. Pat. App. & Int. 1986). Lastly, the prior art reference or combination of references must teach or suggest all the limitations of the claims. See *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970).

If a proposal for modifying the prior art in an effort to attain the claimed invention causes the art to become inoperable or destroys its intended function, then the requisite motivation to make the modification would not have existed. See *In re Fritch*, 972 F.2d at 1265 n.12, 23 U.S.P.Q.2d at 1783 n.12972 F.2d 1260, 23 U.S.P.Q. 2d 1780 (Fed. Cir. 1992) ("A proposed modification [is] inappropriate for an obviousness inquiry when the modification render[s] the prior art reference inoperable for its intended purpose."); *In re Ratti*, 270 F.2d 810, 123 U.S.P.Q. 349 (C.C.P.A. 1959) (holding the suggested combination of references improper under 35 U.S.C. § 103 because it "would require a substantial reconstruction and redesign of the elements shown in [a prior art reference] as well as a change in the basic principles under which [that reference's] construction was designed to operate").

Applicants respectfully maintain that the Office has not met the burden the law allocates to it with regard to establishing a *prima facie* case of obviousness. In particular, modifying Uenoyama et al. in an effort to attain Applicant's claimed method would cause the method described by Uenoyama et al., which relies on addition of calcium, to become inoperable. Therefore, the requisite motivation to make the modification, in this case by eliminating the addition of calcium, necessary to arrive at Applicants' claimed method would not have existed.

Diametrically opposite to the teachings of the present invention, Uenoyama et al. describes a method for assaying the amount of trypsin inhibitor in a urine sample that has as its prerequisite the addition of calcium to the assay medium. According to Uenoyama et al., "when the concentration of the calcium mixed in the buffer solution or the like is low, trypsin may be activated by the influence of calcium in the urine sample, so that the observed trypsin activity measurement would indicate a lower value for the urinary trypsin inhibitor concentration than the real value. Furthermore, if an excess amount of calcium is added, it reacts with carbonate ions, phosphate ions and the like present in the urine to produce precipitates, which affect the measurement" (Col. 1:41-49). Uenoyama et al. teaches that by holding the calcium concentration at a constant level in the assay buffer, a reproducible value for trypsin inhibitor is obtained. Uenoyama et al. teaches that calcium must be added to the assay buffer in a range of from 0.15 micromol or more per 1 microgram of trypsin in order for the activity of the trypsin to be constant (Col. 2:38-46). Thus, modifying the Uenoyama et al. composition in an effort to attain Applicant's claimed method would cause the method described by Uenoyama et al., which relies on addition of calcium, to become inoperable. Therefore, according controlling federal case law, Uenoyama et al. does not provide, and in fact teaches away from, the requisite motivation to make the modification, i.e., by eliminating the addition of calcium, . Without showing the requisite motivation, the Office has not met its burden with regard to establishing a *prima facie* case of obviousness.

Briefly, the secondary references, Ausubel and Berry et al., do not cure the deficiencies of Uenoyama et al. Ausubel is a general reference for the ability of a polycarboxylic chelating agent to bind trypsin. Berry et al., like Uenoyama et al., describes that, if the concentration of the interfering ions is known to be relatively constant in the sample being tested, it is possible to

factor out the inhibitory effect of the ions on a particular enzyme activity. Furthermore, Berry et al. also teaches that, if the concentration of the interfering ion is known, "allowance can be made for this by including an appropriate concentration of the interfering ion in standard (calibrating) solution."(Col. 3:62-66) Thus, the combination of the primary and secondary references suggests that interference of calcium ions on enzyme activity is effectively dealt with by adding calcium ions to the standard (control) and sample so that both have the same amount and thus, the effect on enzyme activity is masked. In particular, modifying either Uenoyama et al. or Berry et al. in an effort to attain Applicant's claimed method would render the methods described by the references inoperable. Therefore, the requisite motivation to make the modification, in this case by eliminating the addition of calcium, necessary to arrive at Applicants' claimed method is not provided by any of the references, either singly or combined.

In view of the amendment and arguments above, removal of the rejection of claims 1-4, 7, 9, 15 and 16 under 35 U.S.C. § 103(a) over Uenoyama et al. in view of Ausubel and further in view of Berry et al. is respectfully requested.

Regarding claims 5 and 6

The rejection of claims 5 and 6 under 35 U.S.C. § 103(a) as being unpatentably obvious over Uenoyama et al. in view of Ausubel and Berry et al., as applied to claims 1-4, 7, 9, 15 and 16, and further in view of GB 2,204,398 to May et al., respectfully is traversed.

The Examiner relies on May as teaching a diagnostic test device containing dry test reagents. The Examiner concludes that it would have been obvious to one of ordinary skill in the art to use the device of May et al. to practice the method of Uenoyama et al. in view of Ausubel and Berry et al.

As discussed above, the combination of Uenoyama et al. and either or both of Ausubel and Berry et al. does not teach or suggest the present invention. In particular, modifying the methods of Uenoyama et al. or Berry et al. in an effort to attain Applicant's claimed method would cause the methods described by the references to become inoperable. The requisite motivation to make the modification, in this case by eliminating the addition of calcium, necessary to arrive at Applicants' claimed method, is not provided by the references, either singly or combined. May et al. merely suggests a device containing dry test reagents, but does not cure the deficiencies of the primary and secondary references. The cited combination of prior art does not render the present invention obvious.

In view of the amendment and arguments above, removal of the rejection of claims 5 and 6 under 35 U.S.C. § 103(a) over Uenoyama et al. in view of Ausubel and Berry et al., and further in view of May et al., is respectfully requested.

Regarding claim 10

The rejection of claim 10 under 35 U.S.C. § 103(a) as being unpatentably obvious over Uenoyama et al. in view of Ausubel and Berry et al., as applied to claims 1-4, 7, 9, 15 and 16, in combination with United States Patent No. 6,130,055 to Nanbu et al., respectfully is traversed.

As discussed above, the combination of Uenoyama et al. and Berry et al. does not teach or suggest the present invention. In particular, modifying either of the Uenoyama et al. or the Berry et al. methods in an effort to attain Applicant's claimed method would cause the method described by the references to become inoperable. Therefore, none of the references, either alone or combined, provides the requisite motivation to make the modification, in this case by eliminating the addition of calcium, necessary to arrive at Applicants' claimed method. Nanbu et al. suggests use of L-

amino acids as trypsin substrate in an assay for trypsin inhibitor, but does not cure the deficiencies of the primary and secondary references. The cited combination of prior art does not render the present invention obvious.

In view of the amendment and arguments above, removal of the rejection of claim 10 under 35 U.S.C. § 103(a) over Uenoyama et al. in view of Ausubel and Berry et al., and further in view of Nanbu et al., is respectfully requested.

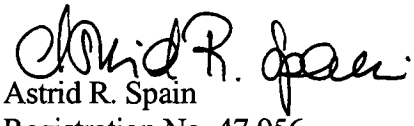
CONCLUSION

In light of the Amendments and Remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to contact the undersigned attorney with any questions related to this application.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

MCDERMOTT WILL & EMERY LLP



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SDO 19347-1.038484.0054